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A LABORATORY INFECTION CAUSED BY A BOVINE STRAIN OF BACILLUS ENTERITIDIS *

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Cases of meat poisoning caused by *Bacillus enteritidis* (Gärtner) or closely allied organisms are very rare in the United States. The rarity of such infections is surprising in the light of numerous observations showing that food-producing animals, as well as experimental animals, are not infrequently infected with these organisms. In recent years, for instance, paratyphoid organisms have been isolated from canary birds and horses, and *B. enteritidis* has been found present in guinea-pigs, rats, dogs (Torrey and Rahe¹), and calves (Meyer, Traum, and Roadhouse²). All of these animals act, in various ways, as sources of infection for man, and in fact the history of meat-poisoning epidemics has shown that they coincide in a most remarkable manner with the consumption of meat from animals infected with septic diseases caused, for the most part, by bacteria which biologically are identical with those isolated from the gastro-intestinal canal of cases of meat poisoning in man. Workers have always been disappointed in not being able to demonstrate experimentally the pathogenicity for men of the animal strains of the paratyphoid-enteritidis group of bacteria, altho descriptions of a few human infections with mouse typhoid bacilli³ have supplied some valuable information concerning the pathogenesis of paratyphoid organisms. In the light of the many undecided questions which such infections present for consideration, it seems worth while to give a description of an interesting laboratory infection which took place during an investigation of the etiology of infectious diarrhea of calves.

THE CASE

History.—A young man, aged 26 years, was infected January 14 while assisting in the feeding of a calf with sterilized milk containing 25 c.c. of a 24-hour-old culture of the paracolon bacillus (*B. enteritidis*, Gärtner, Strain

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¹ Jour. Med. Research, 1912, 27, p. 315.

² Jour. Am. Vet. Med. Assn., 1916, 49, p. 17.

³ See the publications of Trommsdorff, München. Med. Wchnschr., 1903, 50, p. 2092; Meyer, *Ibid.*, 1905, 52, p. 2261; Shibayama, *Ibid.*, 1907, 54, p. 979; and Handson, Williams, and Klein, Brit. Med. Jour., 1908, 2, p. 1547.

1239), which had been isolated 30 days previously. The patient could not recall the manner in which he had contaminated his hands nor did he remember what precautions he had employed for disinfecting them before the evening meal.

From 10 to 12 hours later the patient was seized with severe abdominal cramps, nausea, and diarrhea. By this time he had passed from 3 to 4 semi-solid stools, and by the end of the first 20 hours he had passed 10. The nausea, abdominal cramps, and flatulence continued. The temperature at this time was 101 F., and the patient complained of loss of appetite, headache, and thirst. The tongue was coated, and there were marked fetor oris, and suppression of urine.

Forty-eight hours later the temperature fell to 99.9 F., but the patient still felt weak and depressed. Abdominal pain, tenesmus, and diarrhea continued. During the second 24 hours, he had passed 12 watery stools. These were deeply bile-stained, like rice soup in character, and contained greenish pellets of fecal matter. In the evening the patient took 5 grains of calomel. The diarrhea did not cease, the patient passing 10 more liquid stools in the subsequent 24 hours. These were light-yellow but contained very little mucus. In the evening the patient again took 5 grains of calomel.

On January 18 the patient's temperature again rose to 100 F. He felt weak and thirsty, with a peculiar desire for salt. On this day the patient had passed from 8 to 10 stools. The diarrhea persisted for 2 more days, during which he passed from 6 to 10 stools.

A week following the onset of his illness the patient felt well and ate his regular meals without any ill effect. So far as could be ascertained he had suffered from a chronic mucous colitis, which persisted more or less unaffected by the present illness, as was evidenced by the irregular elimination of mucous casts.

Bacteriologic Examination.—The relation of the gastro-intestinal disturbance to the feeding experiment was unsuspected until 4 days after the onset of the infection. At this time a solid particle of feces was enriched in bile broth and after 12 hours' incubation was plated on litmus-lactose agar. Numerous bluish transparent colonies developed, which were identified as *B. enteritidis* (Gärtner). The various subcultures obtained, behaved in every respect like Calf Strain 1239.² Its characteristic behavior in arabinose broth was noted; indeed, even the first 8 or 10 transplants failed to ferment this pentose. In the white colonies on solid arabinose endo medium there developed, in from about 5 to 7 days, red bud-like daughter colonies consisting of an arabinose "mutant."

The first few transplants of the bacillus were agglutinated only in a dilution of 1:6000 by a serum which agglutinated Strain 1239 in a dilution of 1:10,000. A sample of stool was plated on January 21 directly on litmus-lactose agar. Thirty-seven colonies of *B. enteritidis* and 30 colonies of lactose-fermenting organisms were found in 1 loopful of liquid stool. Stool samples taken on the following days gave positive findings of paracolon bacilli: January 18, 20, 21, 23, 25, 26, 28, 30, and February 1. The samples taken on February 3, 5, 10, May 10, and June 19, were found free of paracolon bacilli, even after an enrichment in bile and in malachite green broth. A large mucous cast eliminated in June proved bacteriologically to be free from *B. enteritidis*.

The pathogenicity of the strain isolated from the laboratory infection is, in some respects, interesting. Mice fed with broth directly by placing 1 drop of a 24-hour-old broth culture on the tongue, either survived or died, with all the lesions of an infection with *B. typhi-murium*, in from 8 to 15 days after

feeding of the bacteria. Mice fed however with meat soiled with a few drops of a suspension of *B. enteritidis*, succumbed regularly to the feeding infection in from 4 to 10 days, the anatomic lesions consisting of a hemorrhagic colitis, splenic tumor, and liver necroses. In a few instances some of the control mice acquired the infection from infected animals occupying the same cage.

Serologic Examination.—The serum of the patient agglutinated neither the typhoid bacillus nor the paracolon bacillus isolated from his stools 6 days after the onset of the gastro-intestinal infection.

On February 3 the serum of the patient was tested against various intestinal organisms, and agglutination occurred in a dilution of 1:1280 only with the paracolon organisms isolated from the patient and with those previously cultured from the calves. No agglutination with one typhoid bacillus strain was obtained.

TABLE 1
RESULTS OF AGGLUTINATION TESTS IN A CASE OF INFECTION WITH *B. ENTERITIDIS*

Antisera	Bacillus of Patient	<i>B. Enteritidis</i> (Strassburg)	<i>B. Enteritidis</i> (A. M. N. H.)
<i>B. typhosus</i> (Cross).....	1:200	1:40	1:60
<i>B. paratyphosus</i> A (polyvalent).....	0	0	1:200
<i>B. paratyphosus</i> A (Strassburg).....	0	0	1:20
<i>B. paratyphosus</i> B (polyvalent, Nos. 4 and 5).....	0	1:2000	1:1000
<i>B. paratyphosus</i> B (homo, Strassburg).....	0	0	0
<i>B. suipestifer</i> (Strassburg).....	0	0	1:100
<i>B. suipestifer</i> V.....	0	1:20	1:20
<i>B. suipestifer</i> (Voldagsen).....	0	0	0
<i>B. suipestifer</i> (typhi-suis).....	0	0	0
<i>B. abortus-equinarius</i>	0	0	0
<i>B. enteritidis</i> (A. M. N. H.).....	1:10,000	1:10,000	1:10,000
<i>B. enteritidis</i> (Strassburg).....	1:20,000	1:40,000	1:10,000
<i>B. enteritidis</i> (guinea-pig, Plotz No. 4).....	1:10,000		
<i>B. enteritidis</i> (No. 5, calf strain 1239).....	1:6000		
<i>B. enteritidis</i> (No. 18).....	1:2000		1:6000
<i>B. typhi-murium</i> (Loeffler No. 1).....	1:10,000	1:8000	1:10,000

Monovalent and polyvalent sera prepared with well-known organisms of the typhoid-paratyphoid groups gave, with the paracolon bacillus of the patient, reactions which are summarized in Table 1. For comparison, 2 other typical strains of *B. enteritidis* are included in the table. The absence of co-agglutination of the patient's strain by paratyphoid sera is interesting in many respects.

Through the careful investigations of Poels and Jensen⁴ it has become established that the so-called paracolon bacilli isolated from calves suffering with infectious diarrhea are related both serologically and biochemically to *B. enteritidis* (Gärtner) and to the ratin bacillus. These findings naturally suggest the possibility that these organisms may also play a part in the etiology of certain enteric fevers in man. The meagerness of studies in this connection may be attributed to the fact that these organisms have been considered to be pathogenic only for man, and that food-producing animals have been thought to become

⁴ Kolle and Wassermann's *Handb. d. pathogen. Microorganismen*, 1913, 6, p. 126.

only accidentally infected with such organisms. But up to within recent years the possibility of the existence of a reverse condition was not entertained. This was largely because of the failure to produce in large animals a paratyphoid-like disease by the inoculation of such organisms found pathogenic for man.

However, the facts concerning the distribution and prevalence of bacteria belonging to the parathyphoid-enteritidis group which have accumulated in the last few years, have led many hygienists to express the belief that all cases of meat poisoning are directly due to intravital contamination of the meat by such bacteria.

Furthermore, carefully conducted inquiries into recent outbreaks of meat poisoning have again failed completely to support this contention. In this connection it is remarkable that very few cases of meat poisoning are reported in the United States, where hog cholera is very prevalent. In this disease of swine, secondary invaders of the paratyphoid group are always present and are doubtless being taken into the human intestinal tract without ill effect. Again, the occurrence of infection in calves with organisms like *B. enteritidis* has been reported in California, and yet no epidemics of meat poisoning have been found traceable to veal infected with *B. enteritidis*.

This may be explained by the fact that in the United States, unlike Belgium and Germany, which, according to Sacquépée,⁵ are "*les terrains de predilection des intoxications alimentaires*," no emergency slaughtering of diseased animals is practiced, and the meat of such animals is rarely consumed. Moreover, the dangers from infected veal are reduced by the strict, tho wasteful, regulations adopted by the various states in the inspection of bob veal and meat in general. Infections from postmortem-contaminated meat are also reduced on account of the limited use of minced, uncooked, or half-cooked meat and the probable absence of a sufficiently large number of human carriers. The yearly increasing improvements in dairy inspection and pasteurization of milk lessen the possibility of infections by this channel.

Probably all these conditions are only in part responsible for the absence of infections with *B. enteritidis* in the United States. Thus far no proof has been brought forward to show with any certainty that the paracolon bacilli or *B. enteritidis* isolated from diseases of calves are always pathogenic for man and, therefore, always capable of causing meat poisoning. In the state of California paracolon-bacillus infections of calves are not rare; thus far, only one epidemic

⁵ *Les empoisonnements alimentaires*, 1909, p. 12.

of meat poisoning is on record (Hogan⁶), and this has not been subjected to a rigorous bacteriologic investigation.

In explanation of these facts two possibilities must be entertained: In the first place, the various strains of *B. enteritidis* may not be identical in their behavior towards man, or it is not unlikely that some predisposing factors, so far unknown, are necessary for successful infections. Secondly, it is possible that epidemics of meat poisoning caused by *B. enteritidis* or paracolon bacilli do occur, but that they are of such mild character as to be rarely brought to public attention.

The first possibility is apparently well supported by the observations of Wiemann⁷ and Rimpau,⁸ who state that veal of animals from which they had isolated paracolon bacilli had been eaten without causing the slightest harm. In support of this, Wiemann reports the following instance: On a farm, over 60 calves suffering from paracolon bacillosis were used as food either after slaughter or after death, and yet no infection resulted.

That the second explanation also has some facts to support it is shown by a statement of Christiansen.⁹ In Denmark, paracolon bacillosis of calves is one of the greatest scourges of the livestock industry, and yet extensive reports of epidemics of meat poisoning are unknown.

Referring to this point Christiansen⁹ in his article on paracolon bacillosis states:

"Even if very serious cases of poisoning are rarely substantiated—which does not mean that they rarely occur—still we have lately seen a case here of mild meat poisoning. Thus in the last few years wholesale cases of meat poisoning have occurred at the hospitals of Copenhagen; fortunately these cases have been of a mild nature in that the disease has been limited to thin purgation a few times together with stomach cramps and in the worst cases vomiting and diarrhea for a day. These cases have always occurred after the eating of a meat course, which in almost all cases, has been of veal. But this does not indicate that paracolon bacillosis caused them, for investigations in regard to the etiology of the cases are not at hand, but they show at any rate that cases of meat poisoning, especially such as are occasioned by the eating of veal, are not so rare, and like cases could very well occur in greater number in the country, without being brought to the knowledge of the public if peculiar circumstances connected with their appearance, in hospitals and like institutions, had but made them better known. It is therefore not right to say that meat poisoning rarely occurs here in this country, nor is it right to use this as an argument for the safety of man against the paracolon

⁶ Bull. California State Board of Health, 1908, 4, p. 67.

⁷ Thesis, University of Bern, 1909, p. 24.

⁸ Klin. Jahrb., 1911, 22, p. 145. Arch. f. Hyg., 1912, 76, p. 9.

⁹ Rep. Serum Lab., Roy. Vet. and Agr. High School, Copenhagen, 1915, 35, pp. 4, 73.

bacilli." (I am indebted to Miss Louise H. Madsen for the translation of the Danish text.)

The necessity of a careful bacteriologic investigation of every gastro-intestinal infection is again suggested by these observations, and the collection of all the data concerning the behavior of paracolon bacilli in man is made imperative.

DISCUSSION

The detailed description of a laboratory infection with *B. enteritidis* isolated from the blood stream of a calf suffering from infectious diarrhea demonstrates the fact that such strains can acquire pathogenicity for man. The course of the infection was severe, probably due to predisposing conditions in the intestinal tract of the patient. This predisposition in form of a mucous colitis is doubtless of considerable importance, since at least 5 other members of the laboratory staff handled, in a very careless manner, feces, organs, and cultures richly impregnated with these paracolon bacilli, and yet no additional infection was brought to our attention. Unfortunately specimens were not obtainable from all the men who handled material contaminated with paracolon bacilli. It would have been interesting to determine the possible occurrence of individuals who could temporarily eliminate the bacilli, as Conradi¹⁰ and Rimpau⁸ were able to show on several occasions. Thus, in the famous meat-poisoning epidemic of St. Johann, numerous persons who had eaten infected meat remained in perfect health and yet eliminated Gärtner bacilli, according to Rimpau. That *B. enteritidis* of animal origin is only pathogenic in man when particularly favorable conditions obtain in the internal tract for their localization, is quite clear from numerous statements and from the evidence presented; it is therefore unnecessary to assume that some strains are more virulent than others. Naturally, passage through man will enhance their pathogenic properties for man, and contact infection, in which milk and other foodstuffs can act as vehicles, will result.

It would appear from our observations that in this instance the introduction of heat-resistant toxins together with the bacteria did not play a very important part in the infection. The toxin produced in the broth was considerably diluted with milk and it is proper to assume that the bacteria alone were taken into the intestinal tract of the patient.

¹⁰ Klin. Jahrb., 1909, 21, p. 421.

According to the experiments on mice the addition of meat to the paracolon bacilli enhances the chances for a successful infection. Probably the toxins which are more extensively produced in meat than in other media, as well as the catarrhal inflammation which results from a diet of raw meat in mice, may be the predisposing factors for the infection.

The virulence of the paracolon organisms was also not particularly high for calves; one feeding experiment did not result in the death of the animal and it was noted that several calves recovered spontaneously from contact infection contracted under natural conditions.

The course of the laboratory infection corresponded well with the typical gastro-intestinal form of paratyphoid infection. Complete recovery resulted in less than 2 weeks. The causative micro-organisms disappeared entirely from the intestinal canal in 20 days after the infection. Repeated stool and numerous cast-examinations gave always negative results after February 3. This observation confirms the observations by Rimpau and others in numerous epidemics, that chronic carriers of *B. enteritidis* do not develop as the result of meat poisoning.

The positive agglutination reaction with the serum of the patient is further proof of the etiologic relation of the calf strain to the infection. The observation that the serum failed to co-agglutinate two strains of *B. typhosus* is, in the light of Langkau's¹¹ work, very suggestive. Bacteria of the Gärtner group always have the tendency to be co-agglutinated by a typhoid serum, even in high dilutions, and in contrast with sera in paratyphoid infections, sera of patients infected with *B. enteritidis* in most instances agglutinate *B. typhosus* (Rimpau¹²). Furthermore, Langkau was able to show that paracolon strains from calves are not co-agglutinated by typhoid- or paratyphoid-immune sera, a condition which is always characteristic of strains of *B. enteritidis* from man, and that this behavior gives a means of differentiating the various types of *B. enteritidis*. The agglutination tests in Table 1 apparently support his findings with the exception that a typhoid serum co-agglutinated the human as well as the calf strain (not tabulated, for the sake of brevity) of *B. enteritidis*. On the other hand, the paratyphoid and suipestifer sera did not agglutinate the paracolon strains.

¹¹ Thesis, Leipsig, 1909.

¹² München. med. Wehnschr., 1909, 56, p. 1843.

So far as we are aware, this is the first instance reported in the literature in which it has been demonstrated that a strain of *B. enteritidis* pathogenic for an animal can, in a particularly predisposed human subject, cause the typical symptoms of meat poisoning. Such susceptibility of the individual doubtless plays an important rôle under practical epidemiologic conditions of meat poisoning in transforming the strain of paracolon bacilli pathogenic for animals into one pathogenic for man, for as a rule the strains of *B. enteritidis* isolated from calves, guinea-pigs, and dogs are of low virulence and, according to a few scattered observations, do not possess the high pathogenicity for man characteristic of the true meat-poisoning organisms.

CONCLUSIONS

This paper presents clinical, bacteriologic and serologic observations of an accidental laboratory infection. A young man who apparently was predisposed to the infection on account of a chronic mucous colitis developed a severe gastro-interitis 10 hours after having handled a bottle of sterilized milk which was artificially contaminated with a culture of *B. enteritidis* (Gärtner). The strain responsible for the infection had been isolated from the heart blood of a calf which had succumbed to infectious diarrhea. Evidence is presented to show that a recently isolated strain of *B. enteritidis* pathogenic for animals may differ from a strain pathogenic for man in its inability to be co-agglutinated by paratyphoid or suipestifer sera.